

### Amendments to the Claims

#### **1-22. (Cancelled)**

**23. (New)** A compound selected from the group consisting of:

N<sup>a</sup>-[4-(Hydroxyamino)-2(R)-isobutyl-3(RS)-methylsuccinyl]-N<sup>e</sup>-acetimidoyl-L-lysine N-methylamide · 1 acetate,

N<sup>a</sup>-[4-(Hydroxyamino)-2(R)-isobutyl-3(RS)-methylsuccinyl]-4'-aminomethyl-L-phenylalanine N-methylamide · 1 acetate,

N<sup>a</sup>-[4-(Hydroxyamino)-2(R),3(R or S)-diisobutylsuccinyl]-L-arginine N-methylamide · 1 acetate,

N<sup>a</sup>-[4-(Hydroxyamino)-2(R)-isobutyl-3(RS)-methylsuccinyl]-L-arginine N-methylamide · 1 acetate,

N<sup>4</sup>-[3-Guanidino-1(S)-methylcarbamoylpropyl]-N<sup>1</sup>-hydroxy-3(R)-isobutyl-2-(RS)-(3-phenylpropyl)succinamide · 1 acetate,

N<sup>4</sup>-[3-Guanidino-1(S)-methylcarbamoylpropyl]-N<sup>1</sup>-hydroxy-3(R),2(RS)-diisobutylsuccinamide · 1 acetate,

N<sup>4</sup>-[3-Guanidino-1(S)-methylcarbamoylpropyl]-N<sup>1</sup>-hydroxy-3(R)-isobutyl-2(R or S)-methylsuccinamide · 1 acetate,

N<sup>a</sup>-[4-(Hydroxyamino)-2(R)-isobutyl-3-(RS)-methylsuccinyl]-L-ornithine N-methylamide · 1 acetate,

N<sup>a</sup>-[4-(Hydroxyamino)-2(R)-isobutyl-3(RS)-(3-phenylpropyl)succinyl]-N<sup>e</sup>-acetimidoyl-L-lysine N-methylamide · 1 acetate,

N<sup>a</sup>-[4-(Hydroxyamino)-2(R)-isobutyl-3(R or S)-methylsuccinyl]-4'-[trimethyl bis(phosphono)methylimino]-L-phenylalanine N-methylamide · 1 sodium salt,

N<sup>a</sup>-[4-(Hydroxyamino)-2(R)-isobutyl-3(RS)-methylsuccinyl]-4'-[tetraethyl bis(phosphono)methylimino]-L-phenylalanine N-methylamide,

N<sup>a</sup>-[4-(Hydroxyamino)-2(R)-isobutyl-3-(RS)-methylsuccinyl]-4'-[triethyl bis(phosphono)methylimino]-L-phenylalanine N-methylamide · 1 sodium salt,

N<sup>a</sup>-[4-(Hydroxyamino)-2(R),3(RS)-diisobutylsuccinyl]-4'-aminomethyl-L-phenylalanine N-(2-hydroxyethyl)amide · 1 acetate,

N<sup>a</sup>-[4-(Hydroxyamino)-2(R)-isobutyl-3(R or S)-(3-phenylpropyl)succinyl]-N<sup>e</sup>-acetimidoyl-L-lysine N-(2-hydroxyethyl)amide · 1 acetate,

N<sup>a</sup>-[4-(Hydroxyamino)-2(R)-isobutyl-3(R or S)-methylsuccinyl]-L-ornithine N-cyclopropylamide · 1 acetate, and

N<sup>a</sup>-[4-(Hydroxyamino)-2(R)-isobutyl-3(RS)-methylsuccinyl]-L-lysine N-methylamide · 1 acetate.

**24. (New)** A compound selected from the group consisting of:

N<sup>a</sup>-[4-(Hydroxyamino)-2(R)-isobutyl-3(R or S)-methylsuccinyl]-4'-acetimidoyliminomethyl-L-phenylalanine N-methylamide · 1 acetate,

N<sup>a</sup>-[4-(Hydroxyamino)-2(R)-isobutyl-3(R or S)-methylsuccinyl]-4'-acetimidoyliminomethyl-L-phenylalanine N-(morpholin-4-yl)-amide · 1 acetate,

N<sup>a</sup>-[4-(Hydroxyamino)-2(R)-isobutyl-3(S)-hydroxysuccinyl]-4'-acetimidoyliminomethyl-L-phenylalanine N-methylamide · 1 acetate,

N<sup>a</sup>-[4-(Hydroxyamino)-2(R)-isobutyl-3(RS)-(3-phenylpropyl)-succinyl]-N<sup>e</sup>-acetimidoyl-L-lysine N-(2-N', N'-dimethylaminoethyl)amide · 2 acetate,

N<sup>a</sup>-[4-(Hydroxyamino)-2(R)-isobutyl-3(RS)-methylsuccinyl]-N<sup>e</sup>-propionimidoyl-L-lysine N-methylamide · 1 acetate,

N<sup>a</sup>-[4-(Hydroxyamino)-2(R)-isobutyl-3(RS)-[3-(4'-guanidinophenyl)propyl]succinyl]-L-ornithine-N-methylamide · 2 acetate,

N<sup>a</sup>-[4-(Hydroxyamino)-2(R)-isobutyl-3(R or S)-(3-phenylpropyl)succinyl]-4'-aminomethyl-L-phenylalanine N-methylamide · 1 acetate,

N<sup>a</sup>-[4-(Hydroxyamino)-2(R)-isobutyl-3(R or S)-(p-aminomethylbenzyl)succinyl]-L-ornithine N-methylamide · 2 acetate,

N<sup>a</sup>-[4-(Hydroxyamino)-2(R)-isobutyl-3 (R or S)-(p-aminomethylbenzyl)succinyl]-4'-aminomethyl-L-phenylalanine N-methylamide · 2 acetate,

N<sup>a</sup>-[4-(Hydroxyamino)-2(R)-isobutyl-3(R or S)-[p-(p-toluene-sulfonamidomethyl)benzyl]succinyl]-L-arginine N-methylamide · 1 acetate,

N<sup>a</sup>-[4-(Hydroxyamino)-2(R)-isobutyl-3(R or S)-(p-phthalimidomethylbenzyl)succinyl]-L-arginine N-methylamide · 1 acetate,

N<sup>a</sup>-[4-(Hydroxyamino)-2(R)-isobutyl-3(R or S)-(p-methane-sulfonamidomethylbenzyl)succinyl]-L-arginine N-methylamide · 1 acetate,

N<sup>a</sup>-[4-(Hydroxyamino)-2(R)-isobutyl-3(R or S)-(2-phenoxyethyl)succinyl]-L-arginine N-methylamide · 1 acetate,

N<sup>a</sup>-[4-(Hydroxyamino)-2(R)-isobutyl-3(R or S)-(3-cyclohexylpropyl)succinyl]-L-arginine N-methylamide · 1 acetate, and

N<sup>a</sup>-[4-(Hydroxyamino)-2(R)-isobutyl-3(R or S)-[3-(p-aminomethylphenyl)propyl]succinyl]-L-lysine N-methylamide · 2 acetate.

**25. (New)** A compound selected from the group consisting of:

N<sup>a</sup>-[4-(Hydroxyamino)-2(R)-isobutyl-3(R or S)-[2-(2-ethoxyethoxy)ethyl]succinyl]-L-lysine N-methylamide,

N<sup>a</sup>-[4-(Hydroxyamino)-2(R)-isobutyl-3(R or S)-[3-(p-carboxyphenyl)propyl]succinyl]-L-lysine N-methylamide,

N<sup>a</sup>-[4-(Hydroxyamino)-2(R)-isobutyl-3(R or S)-(8-hydroxyoctyl)succinyl]-L-lysine N-methylamide · 1 acetate,

N<sup>a</sup>-[4-(Hydroxyamino)-2(R)-isobutyl-3(R or S)-(2-n-butyloxyethyl)succinyl]-L-lysine N-methylamide · 1 acetate,

N<sup>a</sup>-[4-(Hydroxyamino)-2(R)-isobutyl-3(R or S)-(2-isobutyloxyethyl)succinyl]-L-lysine N-methylamide · 1 acetate,

N<sup>a</sup>-[4-(Hydroxyamino)-2(R)-isobutyl-3(R or S)-[3-(m-methoxycarbonylphenyl)propyl]succinyl]-L-lysine N-methylamide · 1 acetate,

N<sup>a</sup>-[4-(Hydroxyamino)-2(R)-isobutyl-3(R or S)-[3-(p-hydroxyphenyl)propyl]succinyl]-L-lysine N-methylamide · 1 acetate,

N<sup>a</sup>-[4-(Hydroxyamino)-2(R)-isobutyl-3(R or S)-[3-(m-carboxyphenyl)propyl]succinyl]-L-lysine N-methylamide · 1 acetate,

N<sup>a</sup>-[4-(Hydroxyamino)-2(R')-isobutyl-3(R or S)-methylsuccinyl]-N<sup>ε</sup>-benzimidoyl-L-lysine N-methylamide · 1 acetate,

N<sup>4</sup>-[3-Amino-1(S)-methylcarbamoylpropyl]-N<sup>1</sup>-hydroxy-2(R or S)-[3-(p-aminomethylphenyl)propyl]-3(R)-isobutylsuccinamide · 2 acetate,

N<sup>a</sup>-[4-(Hydroxyamino)-2(R)-isobutyl-3(R or S)-[3-(p-amino-methylphenyl)propyl]succinyl]-L-ornithine N-methylamide · 1 acetate,

N<sup>a</sup>-[4-(Hydroxyamino)-2(R)-isobutyl-3(R or S)-[3-(p-guanido-methylphenyl)propyl]succinyl]-L-ornithine N-methylamide · 2 acetate,

N<sup>a</sup>-[4-(Hydroxyamino)-2(R)-isobutyl-3(R or S)-[3-(3,4,4-trimethyl-2,5-dioxo-imidazolidin-1-yl)propyl]succinyl]-L-lysine N-methylamide,

N<sup>a</sup>-[4-(Hydroxyamino)-2(R),3(RS)-diisobutylsuccinyl]-4'-acetimidoyliminomethyl-L-phenylalanine N-(2-hydroxyethyl)amide · 2 acetate, and

N<sup>a</sup>-[4-(Hydroxyamino)-2(R)-isobutyl-3(R or S)-[3-(p-aminophenyl)propyl]succinyl]-N<sup>ε</sup>-acetimidoyl-L-lysine N-(2-N', N'-dimethylaminoethyl)amide · 3 acetate.

**26. (New)** A method for preventing or treating a disease or disorder associated with tissue degradation, which comprises administering a therapeutically effective amount of the compound according to claim 23 to a patient in need thereof.

**27. (New)** A method for preventing or treating a disease or disorder associated with tissue degradation, which comprises administering a therapeutically effective amount of the compound according to claim 24 to a patient in need thereof.

**28. (New)** A method for preventing or treating a disease or disorder associated with tissue degradation, which comprises administering a therapeutically effective amount of the compound according to claim 25 to a patient in need thereof.

### **REMARKS**

Favorable reconsideration is respectfully requested in view of the foregoing amendments and following remarks.

Claims 1-22 are cancelled without prejudice.

New claims 23-28 are added. New claims 23-25 are supported by the compounds recited on pages 64-76 of the specification. Specifically, claim 23 is limited to compound numbers 22-30 and 32-38. Claim 24 is limited to compounds numbers 41-52, 54-55 and 61. Claim 25 is limited to compound numbers 66-72, 75, 77-78, 80-82 and 91-92. New claims 26-28 correspond to non-elected claim 8. Rejoinder of this method claim is respectfully solicited upon an allowance of the product claims 23-25.

Turning to the Official Action, claims 4-7 and 16-22 were rejected under 35 USC 112, first paragraph, on the basis that the specification is only enabling for the compounds shown in Tables 1-3, and is not enabling for the scope of the rejected claims.

The rejected claims have been cancelled without prejudice and new claims 23-25 have been added. New claims 23-25 have been drafted as suggested by the Examiner. Specifically, claims 22-28, 30, 32-37, 41-42, 44, 46-47, 50-52, 54-55, 61, 67-72, 78, 80-82 and 91 are shown in one or more of Tables 1-3.

The claims have also been drafted to include a limited number of compounds which are not shown in Tables 1-3 but have similar structures to the compounds listed in Tables 1-3. Accordingly, one skilled in the art would have a reasonable expectation that such compounds would have a similar activity to the listed compounds. These compounds are compound numbers 29, 38, 43, 45, 48-49, 66, 75, 77 and 92.

In view of the foregoing, it is respectfully submitted that the rejection of the claims under 35 USC 112, first paragraph, as applied to the new claims has been overcome.

The new claims are also deemed to overcome the rejection of claims 4-7 and 16-22 under 35 USC 102 as anticipated by Fujisawa, JP 8-53403. The cited reference fails to disclose or suggest any compound according to the new claims.

Favorable reconsideration and allowance is thus respectfully solicited.

Respectfully submitted,

Tetsunori FUJISAWA et al.

By: Warren M. Cheek, Jr.  
Warren M. Cheek, Jr.  
Registration No. 33,367  
Attorney for Applicants

WMC/dlk  
Washington, D.C. 20006-1021  
Telephone (202) 721-8200  
Facsimile (202) 721-8250  
October 14, 2003